39. (amended) A pharmaceutical composition comprising a ligand according to claim 27 and optionally a pharmaceutically acceptable carrier, diluent, excipient or adjuvant or any combination thereof.

40. (amended) A pharmaceutical composition comprising a modulator according to claim 1 either alone or with other active substances.

41. (amended) A method of treating a disease associated with a mannosidase II in a cellular organism, comprising:

(a) administering a pharmaceutical composition according to claim 39; and

(b) activating or inhibiting a mannosidase II to treat the disease.

42. (amended) A method of treating and/or preventing a disease comprising administering a ligand according to claim 27.

43. (amended) A method of determining the secondary and/or tertiary structures of a polypeptide with unknown structure comprising the step of using a crystal according to claim 1.

48. (new) A method of treating and/or preventing a disease comprising administering a pharmaceutical composition according to claim 39 to a mammalian patient.

REMARKS

The above preliminary amendment is made to remove multiple dependencies from claims 6, 17, 23-25, 27, 29, 32-43 and to add new claim 48.

Applicants respectfully request that the preliminary amendment described herein be entered into the record prior to calculation of the filing fee and prior to examination and consideration of the above-identified application.

If a telephone conference would be helpful in resolving any issues concerning this communication, please contact Applicants' primary attorney-of record, Douglas P. Mueller (Reg. No. 30,300), at (612) 371.5237.

Respectfully submitted,

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By _____
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6. A crystal according to claim 1[or 2], comprising a complex between a mannosidase II ligand-binding domain and at least one ligand.

17. A crystal according to [any preceding]claim 1, wherein the crystal has $P2_1$ symmetry.

23. A computer readable medium having stored thereon: the structure of a crystal according to [any of]claim[s] 1[to 21].

24. Machine readable media encoded with data representing the structural coordinates of a crystal or ligand binding domain according to [any of the preceding]claim[s] 1.

25. A method of screening for a ligand capable of binding a mannosidase II ligand binding domain, comprising the use of a crystal according to [any of]claim[s] 1[to 21].

27. A ligand identified by a method according to claim 25[or 26].

29. A modulator of the activity of a mannosidase II derived from a crystal as claimed in [any of the preceding]claim[s] 1.

32. A method for identifying a potential modulator of a mannosidase II function comprising the steps:

(c) docking a computer representation of a test compound from a computer data base with a computer representation of a crystal of a mannosidase II as claimed in [the preceding]claim[s] 1, to obtain complexes;

(d) determining conformations of complexes with a favourable geometric fit and favourable complementary interactions; and

identifying a conformation of a compound that best fits the selected site as a potential modulators of the mannosidase II.

33. A method for identifying a potential modulator of a mannosidase II function comprising the steps:

(c) modifying a computer representation of a test compound complexed with a crystal of a ligand binding domain of a mannosidase II as described in [amy of the preceding]claim[s] 1, by deleting or adding a chemical group or groups;

(d) determining a conformation of the complex with a favourable geometric fit and favourable complementary interactions; and

identifying a compound that best fits the binding site as a potential modulator of a mannosidase II.

34. A method for identifying a potential modulator of a mannosidase II function comprising the steps:

(b) selecting a computer representation of a test compound complexed with a crystal of a ligand binding domain of a mannosidase II as defined in [the preceding]claim[s] 1; and

searching for molecules in a data base that are similar to the test compound using a searching computer program, or replacing portions of the test compound with similar chemical structures from a data base using a compound building computer program.

35. A modulator of a mannosidase II identified by a method according to [any of the preceding]claim[s] 1.

36. A modulator of a mannosidase II based on the three-dimensional structure of an inhibitor's spatial association with a crystal as claimed in [any of the preceding]claim[s] 1.

37. A method for designing potential inhibitors of a mannosidase II comprising the step of using the structural coordinates of a mannosidase II inhibitor defined in relation to its spatial association with a crystal of a mannosidase II or a ligand binding domain thereof according to [any of the preceding]claim[s] 1, to generate a compound that is capable of associating with the mannosidase II or ligand binding domain thereof.

38. The use of a ligand according to claim 27[or 28], in the manufacture of a medicament to treat and/or prevent a disease in a mammalian patient.

39. A pharmaceutical composition comprising a ligand according to [any of]claim[s] 27[or 28] and optionally a pharmaceutically acceptable carrier, diluent, excipient or adjuvant or any combination thereof.

40. A pharmaceutical composition comprising a modulator according to [any of the preceding]claim[s] 1 either alone or with other active substances.

41. A method of treating a disease associated with a mannosidase II in a cellular organism, comprising:

(b) administering a pharmaceutical composition according to claim 39[or 40]; and

(b) activating or inhibiting a mannosidase II to treat the disease.

42. A method of treating and/or preventing a disease comprising administering a ligand according to claim 27[or 28 and/or a pharmaceutical composition according to claim 39 or 40 to a mammalian patient].

43. A method of determining the secondary and/or tertiary structures of a polypeptide with unknown structure comprising the step of using a crystal according to [any of]claim[s] 1[to 21].